



PATENT
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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Richard F Selden et al.

Art Unit: 1636

Serial No.: 09/328,130

Examiner: K. Katcheves

Filed: June 8, 1999

Cust. No.: 21559

Title: In Vivo Production and Delivery of Erythropoietin or Insulinotropin for Gene Therapy

Assistant Commissioner for Patents
Washington, D.C. 20231

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PRELIMINARY REMARKS

Prior to examination of the continued prosecution application that was filed in connection with the above-captioned case on February 7, 2002, kindly consider the following Remarks.

In an Office Action that was mailed on August 7, 2001 in connection with the above-captioned case, the only outstanding rejection was a provisional obviousness-type double patenting rejection over U.S. Serial No. 09/354,883 (the "'883 application"), which has since issued as U.S. Patent No. 6,303,379 B1 (the "'379 patent"). In that rejection, the Examiner noted that the claims of the '883 application were drawn to

primary or secondary cells containing nucleic acid molecules encoding a therapeutic product, as well as methods of producing such cells, and that the present claims differed from those of the '883 application only in specifying that the therapeutic product is erythropoietin. The Examiner further stated that the claims of the present application would have been obvious over the '883 claims, because those of ordinary skill in the art were aware that erythropoietin is a therapeutic product. A rejection for obviousness-type double patenting over the '379 patent should not be made in the present application for the following reasons.

The fact that a protein is known to be therapeutic does not necessarily mean that it would be obvious to administer the protein using an *in vivo*, cell-based approach, such as that in which the cells of the present invention can be used. This approach to therapy simply is not appropriate for the administration of certain proteins. For example, it is imperative that certain therapeutic proteins be administered on a very short-term basis only. Continued production of such proteins in a patient after the condition intended to be treated has been alleviated, as could occur using *in vivo*, cell-based therapy methods, could be dangerous. For example, albumin is frequently administered on a short-term basis to accident victims who have experienced blood loss, in order to increase their serum protein levels. Administration of albumin beyond the period of the initial trauma, however, can lead to serious problems, such as impairment of heart function. Thus, albumin administration is not amenable to *in vivo*, cell-based therapy of trauma.

Prior to the present invention, it was thought that, as was the case for albumin and many other proteins, erythropoietin was to be administered by physicians only in a tightly controlled manner. It was thought that prolonged administration of erythropoietin, which results in increased hematocrit levels, would increase a patient's risk of heart attack and stroke. Thus, clinicians were very cautious about the amounts of erythropoietin that they administered, and certainly would not have been motivated to administer erythropoietin using *in vivo*, cell-based therapy methods. Consistent with this prejudice, prior to the present invention, administration of erythropoietin to patients using *in vivo*, cell-based therapy methods had never been suggested, let alone attempted. Nothing in the record or in any document of which applicants are aware suggests that those persons and companies with an enormous academic or financial stake in erythropoietin held any notion that *in vivo*, cell-based delivery was a viable strategy for erythropoietin therapy. Indeed, all of the evidence demonstrates the opposite: a universal commitment to the injected erythropoietin approach, to the exclusion of other approaches. For example, Amgen Corporation possessed the erythropoietin gene since as early as 1983, published on the gene, and filed a number of patent applications relating to the erythropoietin gene. Yet in not a single one of these documents did Amgen, with its enormous incentive to optimize erythropoietin therapy, make the slightest mention of even the possibility of erythropoietin *in vivo*, cell-based therapy prior to applicants' disclosure. The possibility of such therapy simply was not mentioned in any scientific literature. It necessarily

follows that the presently claimed primary and secondary cells stably transfected with the erythropoietin gene, which are to be used *in vivo* therapy methods, would not have been obvious at the time of applicants' invention. A rejection for obviousness-type double patenting over the '379 patent should therefore not be made in the present application.

CONCLUSION

Applicants submit that the claims are in condition for allowance, and such action is requested. If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: January 21, 2003

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